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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/927,038	08/09/2001	Hisatomi Ito	NANP110US	4720

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EXAMINER	
DELACROIX MUIRHEI, CYBILLE	
ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 12/17/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/927,038	ITO ET AL.	
	Examiner	Art Unit	
	Cybille Delacroix-Muirheid	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *Oct. 20, 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *4,5,9-12,14 and 15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *4,5,11,12,14 and 15* is/are allowed.

6)☒ Claim(s) *9 and 10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Detailed Action

The following is responsive to the amendment received Oct. 20, 2003.

Claims 1-3, 6-8, 13 are cancelled without prejudice or disclaimer.

Claims 4, 5, 9, 10, 11, 12, 14, 15 are currently pending.

Upon further reconsideration of the pending claims and the prior art, the Examiner respectfully submits the following new ground of rejection.

The finality of the office action mailed is withdrawn in view of the following new ground of rejection.

Allowable Subject Matter

Claims 4, 5, 11, 12, 14, 15 are free from the prior art because the prior art does not disclose or fairly suggest the claimed methods.

New Ground(s) of Rejection

Claim Rejections—35 USC 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

1. Claims 9-10 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the treatment of Alzheimer's dementia and encephalic ischemia, does not reasonably provide enablement for treatment of all neurodegenerative diseases. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Wands, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are: (1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary. When the above factors are weighed, it is the examiner's position that one skilled in the art could not practice the invention without undue experimentation.

(1) The nature of the invention:

The claims are drawn to a method of treating neurodegenerative diseases by administering an effective amount of a citrus extract containing a compound represented by Formula (1).

(2) The state of the prior art

The art recognizes the treatment of neurodegenerative diseases such as Alzheimer's disease, Huntington's disease etc., wherein the therapeutic approach focuses on the treatment of symptoms. Standaert et al. teach that although each disorder has a characteristic pattern of neuronal degeneration, the effectiveness of symptomatic therapies differ among the disorders. Please see Standaert et al., Goodman & Gilman's, Pharmacological Basis of Therapeutics, page 503, abstract.

(3) The relative skill of those in the art

The relative skill of those in the art is high.

(4) The predictability or unpredictability of the art

The unpredictability of the pharmaceutical and chemical art is high.

(5) The breadth of the claims

The claims are broad and encompass the treatment of numerous neurodegenerative disorders.

(6) The amount of direction or guidance presented

Applicant's specification provides guidance for and is only enabled for the use of polyalkoxyflavonoid compounds to extend neurite growth thereby treating neurodegenerative disorders such as Alzheimer's dementia and encephalic ischemia. However, the specification provides no guidance, to enable one of ordinary skill in the art to treat "neurodegenerative diseases", which as stated above is broad and encompasses numerous disorders.

(7) The presence or absence of working examples

The examples in Applicant's specification describe using the claimed compounds in extracts for extending neurites in cells isolated from rats. Please see the Examples.

(8) The quantity of experimentation necessary

Since (1) the effectiveness of symptomatic therapies differs from disorder to disorder, (2) Applicant's specification only provides data for inducing neurite growth in cells isolated from rats and (3) due to the scope of the claimed method, one of ordinary skill in the art would be burdened with undue experimentation to determine the pharmacological parameters i.e. dosage, etc. of the claimed compounds necessary to

enable one of ordinary skill in the art to effectively treat all of the disorders encompassed by the claimed method.

Claim Rejections—35 USC 103(a)

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

2. Claims 9-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wenzel et al., US 2001/0046963 A1 (already of record).

Wenzel et al. disclose a method for treating Alzheimer's disease comprising administering effective amounts of a compound such as tangeretine. Please see [0001]; [0024]; [0056].

Wenzel et al. does not teach that the compound is contained in a citrus extract. However, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Wenzel et al. to administer tangeretine in a citrus extract because Wenzel et al. suggest that tangeretine can be added to nutritional substances such as juice extracts from orange and grapefruits. Please see paragraph [0080]. Such a modification would have been motivated by the reasonable expectation of successfully administering the tangeretine to the patient in need thereof.

3. Claims 9-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Castillo et al., US 2001/0047032 A1 in view of Wenzel et al., supra (already of record).

Castillo et al. teach a method for treating Alzheimer's disease or Parkinson's disease by administering effective amounts of a compound gardenin B to a patient in need thereof. Please see the abstract; claims 1 and 29; [0036].

Castillo et al. do not disclose administering tangeretin nor do Castillo et al. teach that the compound gardenin B is contained in a citrus extract. However, the Examiner refers to Wenzel et al., which disclose a method for treating Alzheimer's disease comprising administering effective amounts of a compound such as tangeretine. Please see [0001]; [0024]; [0056]. Wenzel et al. also disclose that the compound may be added

to nutritional substances such as juice extracts from orange and grapefruits. Please see paragraph [0080].

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Castillo et al. to use tangeretine as the active agent because Wenzel et al. disclose and thus suggest to one of ordinary skill in the art that tangeretine would be capable of treating Alzheimer's disease. Additionally, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method by administering the active agents in a citrus extract because Wenzel suggests that juice extracts from grapefruits or oranges may contain the active agents and one of ordinary skill in the art would reasonably expect such citrus extracts to effectively deliver the active agents to the patient in need thereof.

Conclusion

Claims 9-10 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cybille Delacroix-Muirheid whose telephone number is 703-306-3227. The examiner can normally be reached on Mon-Fri from 9:30 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marianne Seidel, can be reached on (703) 308-4725. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

CDM

Dec. 9, 2003

Phyllis Spivack

PHYLLIS SPIVACK
PRIMARY EXAMINER